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EXAMINER	
HENRY, MICHAEL C	

ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/659,063	FINK ET AL.	
	Examiner	Art Unit	
	Michael C. Henry	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-13 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-8 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 9-13 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The following office action is a responsive to a telephone conversation with Holliday Heine on 5/11/04 in which a provisional election was made without traverse to prosecute the invention of Group I, claims 1-8. The response has the following effect:

1 The Election/Restriction has been provided.

2. Claims 1-8, the invention of Group I are prosecuted by the examiner.

   Claims 9-13 are withdrawn.

3. The responsive is contained herein below.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-8, drawn to a method for prophylaxis or treatment of an inflammatory condition, classified in class 514, subclass 46, 47, 886, 921, class 536, subclass 26.4.

II. Claim 9, drawn to a method for testing the effectiveness of a candidate compound for prophylaxis or treatment of an inflammatory condition, classified in class 514, subclass 46, 47, 886, 921, class 536, subclass 26.4, class 424, subclass 9.2, class 436, subclass 500+, class 423, subclass 405.

III. Claim 10, drawn to a method for testing the effectiveness of a candidate compound for prophylaxis or treatment of an inflammatory condition .... For an ability to inhibit permeability, classified in class 514, subclass 46, 47, 886, 921, class 536, subclass 26.4, class 424, subclass 9.2, class 436, subclass 500+.

IV. Claims 11-13, drawn to a method for testing the effectiveness of a candidate compound for prophylaxis or treatment of an inflammatory condition, classified in class 514, subclass 46, 47, 886, 921, class 536, subclass 26.4, class 424, subclass 9.2, class 436, subclass 500+, class 423, subclass 405.

1. Inventions I, II, III and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operation, different functions, or different effects.

2. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

3. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

During a telephone conversation with Holliday Heine on 5/11/04 a provisional election was made without traverse to prosecute the invention of Group I, claims 1-8. Affirmation of this election must be made by applicant in replying to this Office action. Claims 9-13 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Applicant spoke with Michael C. Henry.

Claims 1-13 are pending in application

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The specification, while being enabling for the treatment or prevention of lipopolysaccharide (Lps)-induced mortality in a mice or the partial blocking of the LPS-induced release of TNF-α from RAW cells, does not reasonably provide enablement for the treatment or prophylaxis (or prevention) of inflammatory condition. First, in claim 1, the applicant claims "A method for prophylaxis or treatment of an inflammatory condition, said method comprising the steps of: providing a patient having an inflammatory condition; and administering to said patient a therapeutically effective amount of a composition comprising an NAD-related compound in a form that is accessible to a receptor molecule, conveyed in a pharmaceutically acceptable carrier vehicle, wherein said composition reduces the degree of said inflammatory condition in said patient." The treatment or prophylaxis (or prevention) of inflammatory conditions is not enabled since the said inflammatory conditions does not have a single recognized cause. More specifically, inflammatory conditions encompasses a vast number of ailments or disorders. These conditions include arthritis, pulmonary diseases, psoriasis, colitis, multiple sclerosis, systematic lupus erythematosus,

juvenile diabetes, atherosclerosis, hypothyroidism, tonsillitis, pharyngitis, otitis media, pharyngitis, inflammatory bowel disease, bronchitis, inflammatory diseases of the central nervous system such as algal disorders, bacterial disorders, idiopathic Inflammatory disorders, parasitic encephalomyelitis and viral disorders. In fact, the aforementioned inflammatory conditions, are recognized as having many contributing factors, ranging from hereditary considerations, to lifestyles choices such as the diet and maintenance of bodily healthiness. These are only a few of the factors that promote these conditions in people. Furthermore, the specification does not reasonably provide enablement for the treatment of said condition in a patient (which includes a human). The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict the efficacy of the claimed methods with a reasonable expectation of success. Therefore, the treatment or prophylaxis (prevention) of the said inflammatory condition by one method and one compound is not enabled by the instant disclosure. Dependent claims 2-8, are also not enabled for the treatment or prophylaxis (prevention) of inflammatory conditions in a patient because of the above stated reasons.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "NAD-related compound" in claims 1,7 and 8, is a phrase which renders the claims indefinite. This phrase is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. More specifically, it is unclear what compound is a NAD-related compound much less which compounds are not a NAD-related compound. For example, it is unclear what structural core and/or chemical moieties and/or functional group(s) or must a compound contain to render said compound a NAD-related compound, and what physical and/or chemical properties must this compound possess to in order for one of ordinary skill in the art to determine or assert whether the compound is a related compound to NAD (a NAD-related compound).

The terms "phosphorothioate analogues", "N3'-P5' phosphoroamidate analogues" and "analogues with conformationally locked sugar rings" renders the claims indefinite. More specifically, in the absence of the specific analogues to the chemical core claimed (CCC) or distinct language to describe the structural modifications or the chemical names of the analogues of this invention, the identity of said analogues would be difficult to describe and the metes and bounds of said analogues that applicant regard as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in the claims. Therefore, the identity of this composition component is indefinite. Furthermore, the term " phosphorothioate analogues", "N3'-P5' phosphoroamidate analogues" and "analogues with conformationally locked sugar rings " in all occurrences is seen to be indefinite where applicant fails to provide how the core compound is modified to obtain some analogue version which is intended to be an integral part of the composition claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,6,7 are rejected under 35 U.S.C. 102(b) as being anticipated by Pero et al. (US 6,028,111).

In claim 1 applicant claims "A method for prophylaxis or treatment of an inflammatory condition, said method comprising the steps of: providing a patient having an inflammatory condition; and administering to said patient a therapeutically effective amount of a composition comprising an NAD-related compound in a form that is accessible to a receptor molecule, conveyed in a pharmaceutically acceptable carrier vehicle, wherein said composition reduces the degree of said inflammatory condition in said patient. Pero et al. disclose applicant's method for treatment of an inflammatory condition, said method comprising the steps of: providing a patient (a human) having an inflammatory condition; and administering to said patient (a human) a therapeutically effective amount of a composition comprising β NAD (β nicotinamide adenine dinucleotide), in a pharmaceutically acceptable carrier vehicle (saline solution), wherein said composition reduces the degree of said inflammatory condition in said human (see claim 10 and example 2, col. 5 lines 63 to col. 6, lines 67). It should be noted that Pero et al's composition must be in a form that is accessible to a receptor molecule, since Pero et al's composition is the same as applicant's composition and is used in the same method and produces the same effect.

Claim 6 is drawn to a method of claim 1, wherein said composition is administered to said patient systemically. Pero et al. disclose applicant's method of claim 1, wherein said composition is administered to said patient systemically (see claim 10 and example 2, col. 5 lines 63 to col. 6, lines 67). It should be noted that the examiner considers the manner of administration of said composition to be systematic, since said composition is administered at specific doses (see claim 10 and example 2, col. 5 lines 63 to col. 6, lines 67). In claim 7 applicant claims the method of claim 1, wherein said NAD-related compound is nicotinamide adenine dinucleotide (NAD+) or cyclic adenosine diphosphate ribose (CADPR). Pero et al. disclose applicant's method of claim 1, wherein said NAD-related compound is β NAD (β nicotinamide adenine dinucleotide) which is also known as nicotinamide adenine dinucleotide (NAD+) (see claim 10 and example 2, col. 5 lines 63 to col. 6, lines 67).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5,8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pero et al. (US 6,028,111).

In claim 1 applicant claims "A method for prophylaxis or treatment of an inflammatory condition, said method comprising the steps of: providing a patient having an inflammatory condition; and administering to said patient a therapeutically effective amount of a composition comprising an NAD-related compound in a form that is accessible to a receptor molecule,

conveyed in a pharmaceutically acceptable carrier vehicle, wherein said composition reduces the degree of said inflammatory condition in said patient. Claim 2 is drawn to a method of claim 1, wherein said inflammatory condition is selected from the group consisting of ..... sepsis ..... Dependent claims 3-6 and 8 are drawn to methods involving specific intestinal epithelial inflammation, enteral administration of the composition, and the use of enteric-coated formulation.

Pero et al. disclose a method for treatment of an inflammatory condition, said method comprising the steps of: providing a patient (a human) having an inflammatory condition; and administering to said patient (a human) a therapeutically effective amount of a composition comprising β NAD (β nicotinamide adenine dinucleotide), in a pharmaceutically acceptable carrier vehicle (saline solution), wherein said composition reduces the degree of said inflammatory condition in said human (see claim 10 and example 2, col. 5 lines 63 to col. 6, lines 67). It should be noted that Pero et al's composition must be in a form that is accessible to a receptor molecule, since Pero et al's composition is the same as applicant's composition and is used in the same method and produces the same effect.

The difference between applicant's claimed method and the method of Pero et al. is that applicant claims treatment of specifc inflammatory condition, enteral administration of the composition and the use of enteric-coated formulation.

However, Pero et al. disclose that in general that inflammatory disorders including sepsis can be treated and the administration of the composition can be by an appropriate route such as orally, inraveneously, intramuscularly or subcutaneously (see col. 2, lines 40-65).

It would have been obvious to one having ordinary skill in this art, at the time the claimed invention was made to use the method of Pero et al. for treatment of any inflammatory condition, to administering said composition in commonly suitable formulations (such as enteric-coated formulation), using commonly suitable administrative routes (such as oral routes) based on the type or severity of the condition and the subject or patient been treated, since Pero et al. disclose that said composition can be used to treat inflammations in general by common administrative routes.

One having ordinary skill in this art would have been motivated to use the method of Pero et al. for treatment of any inflammatory condition, to administering said composition in commonly suitable formulations (such as enteric-coated formulation), using commonly suitable administrative routes (such as oral routes) based on the type or severity of the condition and the subject or patient been treated, since Pero et al. disclose that said composition can be used to treat inflammations in general by common administrative routes.

Claims 1-5,8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pero et al. (US 6,028,111) in view of Neurath et al. (Immunobiology, (1997 Dec) 198 (1-3) 91-8).

In claim 1 applicant claims "A method for prophylaxis or treatment of an inflammatory condition, said method comprising the steps of: providing a patient having an inflammatory condition; and administering to said patient a therapeutically effective amount of a composition comprising an NAD-related compound in a form that is accessible to a receptor molecule, conveyed in a pharmaceutically acceptable carrier vehicle, wherein said composition reduces the degree of said inflammatory condition in said patient. Claim 8 is drawn to a method of claim 1, wherein said NAD-related compound is selected from the group consisting of phosphorothioate

analogues, N3'-P5' phosphoroamidate analogues and analogues with conformationally locked sugar rings.

Pero et al. disclose a method for treatment of an inflammatory condition, said method comprising the steps of: providing a patient (a human) having an inflammatory condition; and administering to said patient (a human) a therapeutically effective amount of a composition comprising β NAD (β nicotinamide adenine dinucleotide), in a pharmaceutically acceptable carrier vehicle (saline solution), wherein said composition reduces the degree of said inflammatory condition in said human (see claim 10 and example 2, col. 5 lines 63 to col. 6, lines 67). It should be noted that Pero et al's composition must be in a form that is accessible to a receptor molecule, since Pero et al's composition is the same as applicant's composition and is used in the same method and produces the same effect.

The difference between applicant's claimed method and the method of Pero et al. is that applicant claims the use of specific analogs such as phosphorothioate analogs.

Neurath et al. disclose that antisense phosphorothioate oligonucleotide (a phosphorothioate analogs) can be used to treat patients with chronic intestinal inflammation (see abstract).

It would have been obvious to one having ordinary skill in this art, at the time the claimed invention was made to use the method of Pero et al. in view of Neurath et al. in order to treat chronic intestinal inflammation by administering antisense phosphorothioate oligonucleotide, based on the type or severity of the condition and the subject or patient been treated, since Neurath et al. disclose that said antisense phosphorothioate oligonucleotide can be used to treat intestinal inflammations.

One having ordinary skill in this art would have been motivated to use the method of Pero et al. in view of Neurath et al. in order to treat chronic intestinal inflammation by administering antisense phosphorothioate oligonucleotide, based on the type or severity of the condition and the subject or patient been treated, since Neurath et al. disclose that said antisense phosphorothioate oligonucleotide can be used to treat intestinal inflammations. It should be noted that applicant's

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Henry whose telephone number is 571-272-0652. The examiner can normally be reached on 8:30 am to 5:00 pm; Mon-Fri. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-1235.

MCH

May 12, 2004.

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600